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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/516,493	03/01/2000	Maureen J. Charron	96700/613	3363

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/516,493	CHARRON ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *17,18 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,19-21 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 12/03/01 has been acknowledged.

Election/Restrictions

Applicant's election without traverse of Group-I, Claims 1-16, 19-21 and 25-29 in Paper No. 9 is acknowledged.

Claims 17-18 and 22-24are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Claims 6-11 were amended.
Claims 1-16, 19-21 and 25-29 were examined in this office action.

*If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Rejections - 35 USC § 101 & 35 USC § 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 19-21 and 25-29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 1-16, 19-21 and 25-29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Lack of utility and Enablement rejections are discussed together below:

The instant claims are drawn to a purified and isolated nucleic acid encoding GLUTx, wherein the nucleic acid is derived from Human (SEQ ID NO:6 encoding SEQ ID NO:7), Mouse (SEQ ID NO:9 encoding SEQ ID NO:10) and Rat (SEQ ID NO:11 encoding SEQ ID NO:12). The claims are drawn to an expression vector and host cells containing the GLUTx nucleic acid sequences. In addition the claims are drawn to isolated nucleic acid sequences, which are at least 80-98% homologous with GLUTx nucleic acid sequences.

The specification hypothesize that GLUTx is a novel insulin responsive and glycemia sensitive glucose transporter/sensor/receptor that is instrumental in the maintenance of whole body glucose homeostasis in GLUT4 null mice (spec. page 3, line 13; page 33, line 15). The specification further states that GLUTx could be similar to SNF3 and RGT2 of *Saccharomyces,* which are similar in structure to glucose transporters and can transport glucose but not in sufficient quantities. The specification further teaches that GLUTx polypeptide have 45% and 40% sequence similarity with GLUT4 and SNF3/RGT2 of *Saccharomyces* respectively (spec. page 33, example-6). The specification further disclosed that the preliminary in-situ hybridization studies indicates that GLUTx is expressed in the cerebellum and hippocampus of GLUT4 null mice and these studies suggest that GLUTx may function as glucose sensor or receptor in the brain (spec. page 38, example-9).

The instant invention is not considered to have a specific and/or substantial utility because the specification fails to establish that the disclosed polynucleotide sequences encodes a protein which is a member of glucose transporter/sensor/receptor family as shown by structural and/or functional properties. The recited SEQ ID NO(s) are simply computer-generated hypotheses, wherein no biological function has been established. Since, the instant specification fails to disclose an assay to measure the biological activity of GLUTx polypeptides (as claimed), the only unlimited use for the disclosed polnucloetide sequences would be the determination of what is the biological activity of the encoded by the claimed polynucleotides and further search on how to use the discovered protein activity.

It is known in the art that glucose transporter/sensor/receptor (GLUT) have very divergent functions. Glucose transport across biological membranes requires the presence of specific integral membrane proteins in mammals that fall into two classes i) Na+/glucose cotransporters and ii) SGLT1 and SGLT2. These transporters are involved in glucose absorption into the body, glucose uptake by the brain, storage in liver, insulin-dependent uptake in muscles and adipocytes, and glucose sensing by pancreatic cells. Furthermore, the GLUTs form a family of highly related hexose transport proteins that belongs to a larger sugar transport superfamily consisting of more than 133 members distributed in a wide variety of species. These carrier proteins are characterized by the presence of 12 putative transmembrane segments (Ibberson et al, page 4607. The state of art at the time of filing further teaches that studies performed with knockout mice have revealed the existence of glucose transport activity that could not be accounted for by any known GLUTs (Ibberson et al, JBC, 275(7):4607-4612, 2000). In addition, the amino acid sequences encoding **GLUTX1-consensus sequence** comprises 478 amino acids, whereas the disclosed SEQ ID NO:7 (human) is only 453, SEQ ID NO:10 (mouse) is only 165 and SEQ ID NO:12 (rat) is only 94 amino acid long (see Gene Bank AN: AAB66939 in WO200104145, 2001. *see PTO sequence search report*). It is unclear how the partial sequences (as disclosed) would encode any GLUTx-like activity. At best the instant specification only disclose pieces of GLUTx-like amino acid sequences isolated from hum mouse and rat. However, the specification fails to disclose that these partial sequences have any GLUTx-like activity explicitly or implicitly as putatively considered by the instant specification.

In addition, known glucose transporter (GLUT)1 isoforms differ in their expression in different tissues, in their kinetic characteristics and in their substrate specificity. For example, GLUT1 mediates glucose transport into erythrocytes and through the blood-brain barrier, and appears to provide a basal supply of glucose for most cells. GLUT2 catalyzes glucose uptake into the liver, and is an essential component of the glucose sensing mechanism of the pancreatic cell. GLUT3 is predominantly expressed in neuronal cells, whereas GLUT4 is exclusively found in muscle and adipose tissue. GLUT5 mediates transport of fructose, but probably not glucose, in intestine and spermatozoa. The diverse tissue distribution and the specific functions of GLUT1-GLUT5 appear to indicate that these genes control glucose uptake in mammalian tissues but the possibility that additional unknown sugar transport facilitators also exist (Doege et al, J. Biol. Chem. 275(21):16275-16280, 2000).

The specification alleges that the instant nucleic acid encodes for protein belonging to glucose transporter/sensor/receptor family. However, no sequence comparisons are taught by specification as filed, nor are any specific similarities to other glucose transporter/sensor/receptor expressing proteins (GLUT1-5) are disclosed, such as common areas of conservation. The specification fails to teach that the polypeptide encoded by claimed SEQ ID NO: 7, 10 and 12 have the biological activity of a glucose transporter/sensor/receptor-like protein explicitly or implicitly as putatively considered by the specification. Considering the state of art *(supra),* the only immediate apparent utility for the instant invention would be its further scientific characterization as a putative glucose transporter/sensor/receptor.

In view of the foregoing, one skilled in the art would not readily attribute any particular glucose transporter/sensor/receptor-like activity encoded by the instant nucleic acid in view of the low sequence similarity and the lack of sequence conservation therein. In view of such and the fact that glucose transporter/sensor/receptors differ substantially in activity, it is unclear that any glucose transporter/sensor/receptor could be attributed to the deduced amino acid sequence of the claimed nucleic acid. At best, the Office sequence search using the disclosed amino acid sequences matches with **GLUTX3 consensus sequences** (AN: AAB66941) SEQ ID NO:7 (40%), SEQ ID NO:10 (31%) and SEQ ID NO:12 (42%), but only with very low sequence similarity. Similarly, SEQ ID NO:7 (23%) and SEQ ID NO:12 (30%) matches with GLUTX2 amino acid sequences (AN: AAB66940, AAB66936 respectively), but only with very low

sequence similarity. Further inspection of the comparison shows limited if any areas of conservation between the two sequences. In addition, it is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited SEQ ID NO(s) are simply computer-generated hypothesis because no biological functions have been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. It is unclear whether the nucleic acid encoding the polypeptide of SEQ ID NO:7, 10 and 12 are the proteins that has a biological activity like any known glucose transporter/sensor/receptor. Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene.

In addition, the specification fails to disclose the role of the claimed glucose transporter/sensor/receptor (GLUTx) polypeptide in any disease. It is unclear whether the disease would be the result of the loss of GLUTx bearing polypeptide activity or is the result of altered protein function. It is even unclear whether the treatment of the disease associated with polypeptide as claimed would require increase or decrease in the expression of claimed GLUTx protein. Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. The quantity of experimentation required would include the functional characterization of polypeptide encoded by SEQ ID NO: 7, 10 and 12 as a protein having glucose transporter/sensor/receptor-like activity and use thereof.

Claims 1-16, 20-21 and 25-29 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention of the claims 1-16, 20-21 and 25-29 encompasses any and all natural and non-natural variants of GLUTx nucleotides obtained from any and all organisms. At best, the specification discloses only one variant each for human mouse and rat within the scope of genus comprising the claimed SEQ ID NO:6, 9 and 11. The specification proposes to discover other members of the genus using sequence similarity. However, there is no description of mutational sites that exist in nature, and there is no description how the structure of identified nucleic acid sequences relates to the structure of any strictly neutral alleles. In addition, the glucose transporter/sensor/receptor (GLUTs) included members that would expected to have widely divergent functional properties (*Supra).* The general knowledge in the art glucose transporter/sensor/receptor does not provide any indication as how the structure of one allele is representative of other unknown amino acid sequences having concordant or discordant functions. The commons attributes of all glucose transporter/sensor/receptor are not described, and identifying attributes of individual GLUTx-like protein other than SEQ ID NO:6, 9 and 11 are not described. The nature of glucose transporter/sensor/receptor is that they are variant structures and functions of others (*supra*). At best the specification only disclosed nucleic and amino acid sequences encoding human, mouse and rat GLUTx polypeptide (SEQ ID NO:7, 10, 12). Furthermore, the amino acid sequences encoding GLUTX1-consensus sequence comprises 478 amino acids, whereas the disclosed SEQ ID NO:7 (human) is only 453, SEQ ID NO:10 (mouse) is only 165 and SEQ ID NO:12 (rat) is only 94 amino acid long (see Gene Bank AN: AAB66939 in WO200104145, 2001. *see PTO sequence search report*). At best the instant specification only disclose pieces of GLUTx-like amino acid sequences isolated from hum mouse and rat. It is unclear how the partial sequences (as disclosed) would encode any GLUTx-like activity explicitly or implicitly as putatively considered by the instant specification..

The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In addition possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of

the claimed invention Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

In addition, the instant specification fails to disclose any and all variant of GLUTx polypeptides, which has any glucose transporter/sensor/receptor-like activity from any and all organisms. The invention as claimed encompass nucleic acid sequences, which are alt least 80-98% to the claimed GLUTx sequences. The variation as claimed even encompasses the conserved motifs that are germane to any glucose transporter/sensor/receptor-like activity. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The variants as claimed are simply computer generated hypothesis because no biological functions has been established even for SEQ ID NO:7, 10 and 12. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues *(supra)*. Therefore, the applicant has not presented enablement commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1-16, 19-21 and 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 12 and 19 are indefinite because it is unclear what are the metes and bounds of GLUTx. It is unclear how one knows that a nucleic acid encoding a member of the GLUT-family is GLUTx and not some other GLUT.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 12-13, 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al (EST ID:H34451, ID:H34372, 1998, *see PTO Sequence search report.* and PNAS 92:8303-8307, 1995). The cited art teaches a nucleic acid sequence which matches 99.1% to the nucleic acid sequence of SEQ ID NO:11 and 95.5% with the nucleic acid sequence of SEQ ID NO:9 of instant application. Furthermore, the cited prior art teaches cloning of nucleic acid sequences in a plasmid vector. In addition considering the high sequence similarity, the nucleic acid as disclosed in the prior art would inherently encode a GLUTx like activity, whatever it happens to be. Thus the cited art clearly anticipated the invention of instant claims.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al (GeneBank AN:G20347, 1996, *see PTO sequence search report*). The cited art teaches a nucleic acid probe which would hybridizes to nucleic acid sequence of SEQ ID NO:6. Thus the cited art clearly anticipated the invention as claimed.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al (GeneBank AN:AB005878, 1997, *see PTO sequence search report*). The cited art teaches a nucleic acid probe which would hybridizes to nucleic acid sequence of SEQ ID NO:9. Thus the cited art clearly anticipated the invention as claimed.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al (GeneBank AN:CGRHOD, 1992, see PTO sequence search report 2002). The cited art teaches a nucleic acid probe which would hybridizes to nucleic acid sequence of SEQ ID NO:11. Thus the cited art clearly anticipated the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (EST ID:H34451, ID:H34372, 1998, see PTO Sequence search report 2002. and PNAS 92:8303-8307, 1995) as applied to claims 1-2, 4-5, 12, 20-21 above, and further in view of Ausubel et al (Short Protocols in Molecular Biology, 3rd Edition, Wiley & Sons Inc. 1995, see pages 16.3-5 and 16.58-62)

Lee et al (EST ID:H34451, ID:H34372, 1998, see PTO Sequence search report 2002. and PNAS 92:8303-8307, 1995 teaches a nucleic acid sequence which matches 99.1% to the nucleic acid sequence of SEQ ID NO:11 and 95.5% with the nucleic acid sequence of SEQ ID NO:9 of instant application. Considering the high sequence similarity, the nucleic acid as disclosed in the prior art would inherently encode a GLUTx like activity. In addition, the cited prior art teaches cloning of nucleic acid sequences in a plasmid vector. However, Lee et al does not teach transformed host cells and a method for producing the recombinant GLUTx protein.

Ausubel teaches a method for transforming prokaryotic and eukaryotic host cells with plasmid and viral expression vectors to produce or express the protein of interest. The cited art further teaches that the expressed protein could also be used as an antigen to make antibodies (pages 16.3-5 and 16.58-62).

Thus, it would have been obvious to one ordinary skill in the art at the time of filing to transfect the expression vector as taught by Lee into the prokaryotic and eukaryotic cells host cells as taught by Ausubel to produce the claimed recombinant protein. One would have been motivated to do so because the recombinant proteins could be further used to make antibodies

(see Ausebel). In addition, one would have been also motivated to make the transformed cells (as claimed) to study the role of GLUTx expression in the development neuronal phenotype (see Lee, abstract). One would have a reasonable expectation of success because cloning and gene expression in prokaryotic and eukrayotic is routine in the art. Thus the invention as claimed is *prima facie* obvious in view of cited art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor IremYucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
PATENT EXAMINER

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER